IOM Report – Vaccines & Autism

As you know, vaccine safety concerns are common among both parents and vaccine providers. It seems that hardly a day goes by without some vaccine safety article on television, or in print, or on the Internet. One of the most persistent vaccine safety issues is the allegation of an association between measles vaccine, MMR, thimerosal, and autism. In 2000, the Centers for Disease Control and Prevention and the National Institutes of Health asked the Institute of Medicine to establish an independent expert committee to evaluate evidence regarding whether vaccines cause certain health problems, and to report their conclusions and recommendations.

In its first report in 2001, the Immunization Safety Review Committee reviewed the hypothesized association between measles-mumps-rubella vaccine and autism, which the committee rejected based on the evidence at the time. The second report in 2001 reviewed the hypothesized link between thimerosal-containing vaccines and a broad range of neurodevelopmental disorders including autism. The committee concluded that the evidence available at the time was inadequate to either accept or reject a causal relationship between thimerosal and neurodevelopmental disorders. This means that at that time, with the evidence available, the committee could not conclude one way or the other on the question. In May 2004, the Immunization Safety Review Committee issued its eighth and final report on the issue of vaccines and autism. We asked Dr. Kathleen Stratton, study director for the vaccine safety reports, to tell us about the new report.

Roy: Dr. Stratton, why has the Immunization Safety Review Committee revisited the issue of vaccines and autism?

Stratton: The Immunization Safety Review Committee first reviewed data on the association of MMR vaccine and autism, and thimerosal and neurodevelopmental disorders in 2001. These reviews – particularly that regarding thimerosal - were hampered by a paucity of well-conducted epidemiologic studies at the time. Since 2001 a lot of additional studies have been performed to examine these issues. In the May 2004 report, the committee updated its conclusions and recommendations regarding vaccines and autism based on this new information.

Roy: What new information about thimerosal and autism has become available since 2001?

Stratton: Several recent studies have examined the association between thimerosal-containing vaccines and autism.

Since 2001, three controlled epidemiological studies and two uncontrolled observational studies have been published that have found no evidence of an association between thimerosal-containing vaccines and autism. These studies utilized different methods and examined different populations in Sweden, Denmark, the United States, and the United Kingdom.

Several studies claimed to have found an association between thimerosal containing vaccines and autism. However, all these studies have serious methodological and analytic flaws and so were not helpful in the assessment. Based on this body of evidence, the committee concludes that the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism. This conclusion differs from the committee's finding in its 2001 report on thimerosal containing vaccines and neurodevelopmental disorders. The committee reported then that the evidence was inadequate to accept or reject a causal relationship between exposure to thimerosal from childhood vaccines, and the neurodevelopmental disorders of autism, ADHD, and speech and language delay. The committee's conclusion in 2001 was based on the fact that there were no published epidemiological studies examining the potential association between thimerosal-containing vaccines and neurodevelopmental disorders. the two unpublished, epidemiological studies that were available provided only weak and inconclusive evidence. Furthermore, the conclusion in the 2001 report pertained to a broader set of neurodevelopmental disorders, while this report's conclusion applies *only* to autism.

Roy: The possible relation of MMR vaccine and autism continues to concern parents. What information did the committee review for this part of its report?

Stratton: Since 2001 there have been many investigations into the association between MMR and autism. Fourteen studies have examined this issue, including 9 controlled observational studies, three ecologic studies, and two studies based on a passive reporting system in Finland. These studies have consistently showed evidence of no association between MMR vaccine and autism. Two studies reported an association. However, like the positive thimerosal studies by the same authors, these studies had serious methodologic and analytic flaws and were not useful as far as assessing causality. The original case series reported by Andrew Wakefield in 1998 was also not helpful in our review. Based on this body of evidence, the committee concludes that the evidence favors rejection of a causal relationship between MMR vaccine and autism. This conclusion is consistent with the finding in the committee's previous report on MMR and autism.

The committee also considered the biological mechanisms by which MMR or thimerosal could lead to autism. It's clear from twin and family studies that there is a strong genetic basis for autism. Several investigators have proposed hypothetical biologic mechanism. However the experiments being conducted to support these hypotheses lack relevance to our current understanding of the development of autism. In the absence of evidence that vaccination- either MMR or thimerosal- affects any physiologic or molecular mechanisms that are know to be causally-related to the development of autism, the committee concludes that the hypotheses regarding a link between autism and MMR vaccine and thimerosal-containing vaccines are only theoretical.

The committee believes that future research to find the cause of autism should be directed toward other promising lines of inquiry that are supported by current knowledge and evidence and offer more promise for providing an answer. The committee does not consider a significant investment in studies of the theoretical vaccine-autism connection to be useful at this time. The committee's conclusions of a lack of association between either thimerosal or MMR and autism should be really good news for both parents AND providers. We can continue to protect children with vaccines without the specter of autism over us.

Roy: What policy and research recommendations did the committee make?

Stratton: The committee made a number of recommendations in the areas of policy, surveillance, and epidemiologic research, clinical studies, and communication. First, the committee does *not* recommend a policy review of the licensure of MMR vaccine or of the current schedule and recommendations for giving the MMR vaccine to children. Second, the committee does not recommend a policy review of the current schedule and recommendations for the administration of routine childhood vaccines based on hypotheses regarding thimerosal and autism. Third, the committee recommends that cost-benefit assessments regarding the use of thimerosal-containing versus thimerosal-free vaccines and other biological or pharmaceutical

products, whether in the United States or other countries, should not include autism as a potential risk. The committee heard from some parents of children with ASD who have chosen to rely on chelation therapy as a treatment. The committee saw no scientific evidence that chelation is an effective therapy for ASD, or is even indicated in children with ASD. Chelation therapy is currently indicated only for high dose acute mercury poisoning. Because chelation therapy has potentially serious risks, the committee recommends that it be used only in carefully controlled research settings with appropriate oversight by Institutional Review Boards to protect the interests of the children who participate. Finally, the committee recommends developing programs to increase public participation in vaccine safety research and policy decisions. These programs should also enhance the skills and willingness of scientists and government officials to engage in constructive dialogue with the public about research findings and their implications for policy development. The committee also made several recommendations regarding surveillance of adverse events and following vaccination and epidemiologic research. These include the use of standardized case definitions of autism spectrum disorder and additional investigations into risk factors and biologic markers for autism. Details of these recommendations can be found in the full report. From its inception the Immunization Safety Review Committee has been supportive of ongoing vaccine safety research. The committee is also very supportive of additional research on autism in general. This disease can be devastating to a family. Better understanding of the biology of autism can help point the way to better treatment and, ultimately, to prevention.

Roy: Dr. Stratton, thank you for taking time to share this information with our audience today.

Stratton: My pleasure. Thank you.

The conclusions of the eighth and final report of the IOM Immunization Safety Review Committee were released on May 18, 2004. The full report is being printed now, and should be available from the National Academy of Sciences in the next few weeks. The National Immunization Program has a summary of the report, as well as background on measles vaccine, thimerosal and autism on their website. The website also has fact sheets on the report for both providers and parents. These fact sheets provide background on the Committee, and summarize the evidence supporting the Committee's conclusions. The fact sheets should be helpful for your staff and parents who are concerned about vaccines and autism. We will put a link to the summary materials and fact sheets on our broadcast resources website.